Immunological Nudging

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Contributor: Gysbert van Setten

The constant activation and deactivation of immunological processes in harmony due to physiological processes is the basis of the immunological homeostasis. Activation may be chemical or physical such as by mechano-transduction. The immunological system in a healthy system can never be deactivated, i.e. silenced without increasing the risk for sudden and complete incapacitation and malfunction. The functionality of this system and it's often vital reactivity depends on the immediate "on demand" availability of all major components in the regulatory mechanisms involved. This is only possible by constant and subtle, subclinical activation and deactivation of this system. This is in contrast to the temporary or occasional nudging of immunological reactions that is intended to provoke specific immune responses.

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Immunology is regulated within systems that are fine-tuned in a constant homeostasis. The immune system itself has vital functions for both homeostasis and host defense (Simon 2019) [1]. Biologics responsible for maintenance of a functional homeostatsis in capable systems such as TNF Activity and T cells (Mehta et al. 2018) [2] are key players in immunological nudging and need to be identified. The prerequisites of the ability to react immediately as needed in this system of defense, is a constant availability of regulative mechanisms turning on and off in interaction with each other. Most recently such an ability of a system has been described as anticipatory defense response (Nakao et al. 2020) [3]. However, only by constant availability of all components necessary for effective functionality of each regulatory unit a swift immunological response in full coordination with all regulatory units is possible. This could play an essential role in adaptive immunity considering antiviral response in which t IL-33 is also a crucial amplifier (Zhou et al. 2020) [4]. In contrast to such stimulation as immediate and intense initiation of a response as defense mechanism is the immunological nudging the soft and repeated or constant gentle low degree tickling of a powerful system in the sole purpose that the regulatory systems do not fall asleep. It is suggested to introduce the term immunological nudging, for the constant subclinical external stimuli that keep all components of the system in good functional condition and reactive capacity. Due to the soft push on the activation of auto-regulatory mechanisms, such immunological nudging guarantees the availability of immediate immunological response ability by constantly, usually sub-clinically, activating and silencing each regulatory unit. It is suggested that the constant activation and deactivation of major regulatory circuits in perfect harmony maintains the readiness to immediate immunological reaction. As inflammation and immunology are inseparably linked any chronic or temporary inflammatory reaction also influence the immunological homeostasis and thus contribute to immunological nudging. Even very subtle, subclinical inflammation such as due to attrition (van Setten 2020) [5] could be important. Immunological nudging possibly is a general principle of keeping our immune system awake and responsive to external challenges. Similarities in the animal kingdom might exist. Further studies will show if this ability is dependent or modulated by age, climate, circadian rhythm , medications or disease. For the field of ocular surface inflammation, for example, constant mechanical force exposure, creating attrition could lead to a constant low-level presence of inflammation. Naturally, any additional inflammatory trigger, such as neuro stimulation in dry eye decease, could easily lead to an acceleration of this subclinical inflammation. Only constant subclinical activation of regulatory mechanisms can provide the availability of essential substances needed in the regulatory cascades of immunoresponse. Non-availability or shortage in availability of any component in such a cascade would result in late or non-response and possibly activation of secondary mechanisms with a wider spectrum of not intended effects. This could then, in turn, lead to a possible longer time needed for silencing the system again, allowing the system to re-establish the homeostatic level of activation. Frequency and intensity of immunological nudging may be critical for appropriate functionality; processes of training and adaption may be possible.

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